Annual Report
Division of Endocrinology
Department of Medicine - Jewish General Hospital
April 1, 2009 - March 31, 2010

I HIGHLIGHTS

The Division of Endocrinology and Metabolism has continued its pursuit of excellence in patient care, research and training. The Division has continued to play an active role in joint activities with the other McGill Hospitals counterparts, such as Med-I Endocrine Physiology Course and Calcium Homeostasis, as well as hosting the Lipid-, Thyroid McGill Lectureships, and the newly established McGill/JGH Lecture on Metabolism, supported by a grant from GlaxoSmithKline. Our members continue to teach in McGill Graduate and Undergraduate courses such as Physiology (Tamilia), Advanced Endocrinology (Tamilia) and Neuroendocrinology (Tamilia). With a grant from GlaxoSmithKline, our Division hosted another McGill Lecture (details under Teaching Activities). Members of the Division continue to serve in committees of granting agencies, editorial boards and to participate in other high level academic activities at national and international levels. Members have succeeded in the competing renewal of their grants as well as in obtaining additional support from peer-reviewed granting agencies. Dr. Michael Tamilia has continued to receive the recognition of our young colleagues and students as a truly exceptional teacher. Drs. Tina Kader and Morris Schweitzer continue to be remarkable active in CME activities primarily addressed to general practitioners, internists and specialists. Thus, the JGH Endocrine Division has reached a high profile at the University, National and International levels. In spite of the limited resources and the absence of physical plant, the Metabolic Day Centre under the direction of Dr. Alicia Schiffrin has continued the effort to improve the care of patients with diabetes and bring us to the standards. Dr. Amnon Kahn has successfully reached donors to support our effort in providing state-of-the art treatment and education of patients with Diabetes to palliate the limited resources available for this major current medical problem. He has made arrangements with Montreal Children's Hospital to again access for our patients to insulin pump usage. Overall, the Division of Endocrinology is one of the most, if not the most, active in contributing its staff to teaching (ICMA, ICMB, Physiology) and CTU coverage within the Department of Medicine at the Jewish General Hospital. Our newest recruits John Brent Richards and Agniezska Majdan (Aug. 2009) will continue to perform as superb academic physicians; Dr. Brent Richards has in short order achieved already much acclaim in his young career.

II EVALUATION OF THE PAST ACADEMIC YEAR

1. Teaching activities

Medical Students

Metabolic Bone Disease in Unit 5, Med I; preparation of lecture notes, case study, and quiz for students and organizing small group tutors.
One 1-hour lecture on metabolic bone disorders and two 1.5-hour small group sessions

Residents
(I) Journal Club
(ii) Core lectures in Endocrinology
(iii) Simulated oral examination in Internal Medicine

Postgraduate Students

Advances in Human Genetics: A post graduate course offered by the Department of Human Genetics: Three 1.5-hr lectures on the genetics of metabolic bone diseases.

Endocrine Residents (Fellows) and Medical Residents doing elective rotations participate in all our clinical activities. They are under the direct supervision of the Attending on service. Residents must attend clinics while not busy with the in-patient service. Some clinics are compulsory: Gestational Diabetes, Thyroid, Lipid and Osteoporosis Clinic. Our Division has become very popular for elective rotations among residents and students. All trainees rotating through the Division must attend Endocrine Grand Rounds (every Thursday from 11:30-12:30). This past year we have had an unusually high number of Endocrine Residents, and the same is expected for the next academic year. In addition to McGill Medical Students doing elective rotations, we have received students from UK, Australia, Finland, and Brazil during the last year. Notably, the majority of McGill candidates to McGill Endocrine Residents have come from our Internal Medicine training program over the last several years, a reflection of the positive influence of our staff on the Residents. The McGill Endocrine Teaching Program at large was highly rated by the trainees with our Division receiving the highest ratings in a large number of items, notably conferences, bedside and outpatient teaching, integration with basic sciences. Our weakest mark is on premises and facilities for Endocrine Residents.

In addition to these tutorial activities, our Division offers a yearly cycle of lectures on essential endocrinology for residents and non-endocrinologists in general. Our Division also actively participates in the undergraduate teaching of Endocrine Physiology and Calcium Homeostasis (Med-I Physiology) with 6 of our members being small group tutors this year (Assimakopoulos, Beitel, Kader, Karaplis, Schiffrin, and Trifiro). All GFT's have also been very active on CME accredited activities. Dr. Tina Kader has been traditionally active in CME to various groups of physicians, paramedical personnel, as well as in giving talks to the community at large on prevention of obesity and diabetes. Ms. Joyce Arsenault (Nurse, Certified Diabetes Educator), Ms. Maria Di Narzo (nurse, Certified, Diabetes Educator) and Ms. Sondra Sherman (Dietitian) have worked together with Dr. Tina Kader in this latter endeavour.

The McGill Hospital Endocrine Division hold quarterly combined Endo Rounds, one of which is hosted by our Division. Our Division has for years hosted two major McGill Endocrine lectures, the McGill/Merck Frosst Lipid Lecture and the McGill/Abbott Thyroid Lecture. Invited speakers for the period covered by this report were, respectively, David J. Mangelsdorf, Ph.D., Professor of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center, Rotterdam, The Netherlands. Nearly 5

years ago, we instituted a third Lectureship, the McGill Lecture on Metabolism, with a restricted grant from GlaxoSmithKline. The Fourth McGill/JGH Lecture on Metabolism was given by Michael W. Schwartz, MD, Professor of Medicine, Division of Metabolism, Endocrinology and Nutrition, University of Washington and Harborview Medical Center, Seattle Washington.

In addition to the teaching activities described under Teaching Activities, above, Endocrine Grand Rounds, under the direction of Dr. Mark Trifiro, have continued to be a great success because of the timeliness of the subjects, the sensible balance of basic and clinical science and the quality of the invited speakers. Endo Grand Rounds are given weekly from September to June.

2. Research Activities

Research activities continue in the rise (see individual reports for details).

Karaplis, Andrew C.

2005-2010: Canadian Institutes of Health Research (Total: $606,385)
"PTHRP and osteoblast biology: Relevance to osteoporosis".

2006-2009: Canadian Institutes of Health Research (Total: $336,000) “Molecular genetics of caclitropic hormones”

Trifiro, Mark

2009-2012: Fonds Québecois de la recherche sur la Nature et les Technologies, Operating $48,760/yr (Co-Pi), «Biosenseurs génétiquement modifiés à haute sélectivité et sensibilité »

2009-2012: Canadian Institute for Photonics Innovation (CIPI), $29,900 total,
« Nanoporous silicon catheter device with real-time optical monitoring of bacterial contaminants during hemodialysis »

2009-2011: Animas Corporation $50,000/yr Canadian Artificial Pancreas Project

Beitel, Lenore

2009/12-2010/11: Kennedy’s Disease Association, $10,716 total, “Investigating mechanisms contributing to Kennedy’s disease: Polyglutamine-expanded androgen receptors and the ubiquitin-proteasome system”

Richards, John Brent
2010 : Ministère du développement économique, Innovation et Exportation du Québec. CiPhER : Consortium International pour l’identification des gènes de facture ostéorobotique. Rôle : Principal Investigator. $491,231 over 3 years.

3. Clinical Activities:

Endocrinology is largely an outpatient specialty. Including the Gestational Diabetes Clinic and Bone and Osteoporosis Clinics that do not function in our premises, the number of visits per year exceeded the 20,000. Outpatient clinics are run around the week by GFT's. Non-GFT's run clinics on Monday and Thursday mornings. The increase in the number of patients is still too long. It has been due to space and support personnel constraints that we have not been able to recruit more new members. Constraints also result from the RAMQ that is trying to restrict the number of endocrinologists. This problem has been solved at the expense of physician scientists increasing their clinical hours, reducing their research time. We also have established a triage system to see first those patients in most urgent need (e.g. decompensated diabetics, thyrotoxic patients). To enhance the use of the space, examining space has been arranged in three of the largest physician offices. We have stretched to the limits the secretarial time available, which has not increased in over 6 years in spite the doubling of the numbers of patient visits. Although all staff physicians see patients spanning the whole spectrum of endocrine and metabolic diseases, some clinics are focused on a particular condition, as shown in the table below.

In-patient activities are centered on the Endocrine Consulting Service, attended by our staff physicians in a 2-week rotating schedule through the year. The endocrine service is largely covered by 7 of the 8 GFT's, which burden's them – including the physician scientists- with a minimum of 6 weeks per year. Volume of consults is approximately 1200/year. In addition, our staff is actively involved in CTU rotations. The Division does not have assigned beds and endocrine patients are admitted to general wards.

The Survival Skills Program of self-management education for patients with diabetes has continued to function regularly with private donations. No additional resources have been provided this year for the essential program.

Outpatient Clinics:

Monday AM
Diabetic Clinic (Kader)
General Endocrinology (Schweitzer, Karaplis, Trifiro, Kahn)
Monday PM
General Endocrinology (Karaplis, Assimakopoulos, Schweitzer)

Tuesday AM
Thyroid (Tamilia)
General Endocrinology (Trifiro, Assimakopoulos, Schiffrin)
Tuesday PM
General Endocrinology (Assimakopoulos, Schiffrin, Christopoulos, Richards)

Wednesday AM

General Endocrinology (Kader, Trifiro, Majdan)
Gestational Diabetes (Kader)
Osteoporosis I (Trifiro)
Wednesday PM
General Endocrinology (Christopoulos, Richards, Majdan)
Osteoporosis II (Karaplis)

Thursday AM
General Endocrinology (Schiffrin, Tamilia, Clamen, Kahn, Rizzo, Jukier)
Thursday PM
Lipid Clinic (Schweitzer)
General Endocrinology (Assimakopoulos, Kader)

Friday AM
General Endocrinology (Schiffrin, Schweitzer, Trifiro, Christopoulos, Majdan)

4. Academic Staff

- Dr. Lillian Jukier has become an affiliated endocrinologist in our division and will participate in Consultation Service and specialty clinics.
- Dr. Agnieszka Majdan has been approved at the hospital and university levels and she joined our Division in September 2009.

5. Consulting Activities: None reported

6. Honours, Awards, Prizes

7. Other

Publications

Schweitzer, Morris

--Gottlieb, Bruce, Lorraine E. Chalifour, Benjamin Mitmaker, Nathan Sheiner, Daniel Obrand, Cherrie Abraham, Melissa Meilleur, Tomoko Sugahara, Ghassan Bkaily, and Morris Schweitzer. “BAK1 Gene Variation and Abdominal Aortic Aneurysms.” *Human Mutation* 30.7 (2009):1043-047.

--Schweitzer, Morris, Benjamin Mitmaker, Daniel Obrand, Nathan Sheiner, Cherrie Abraham, Stevan Dostanic, and Lorraine E. Chalifour. “Atorvastatin mediates increases in intralesional BAD and BAK expression in human end-stage abdominal aortic aneurysms.” *Canadian Journal of Physiology and Pharmacology* 87 (2009): 915-22.

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--Schweitzer, Morris, Benjamin Mitmaker, Daniel Obrand, Nathan Sheiner, Cherrie Abraham, Stevan Dostanic, Melissa Meilleur, Tomoko Sugahara, and Lorraine E. Chalifour. "Atorvastatin Modulates Matrix Metalloproteinase Expression, Activity, and Signaling in Abdominal Aortic Aneurysms." *Vascular and Endovascular Surgery* 44.2 (2010): 116-22.

Karaplis, Andrew C.

Refereed papers

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--Bai X, Dinghong Q, Miao D, Goltzman D, Karaplis AC. Klotho ablation converts the biochemical and skeletal alterations in FGF23 (R176Q) transgenic mice to a Klotho-deficient phenotype. Am J Physiol Endocrinol Metab 2009;296:E79-88.

Trifiro, Mark

--Di Fabio F, Alvarado C, Gologan A, Youssef E, Voda L, Mitmaker E, Beitel LK, Gordon PH, **Trifiro M**. Somatic mosaicism of androgen receptor CAG repeats in colorectal carcinoma and normal mucosa from men. J Surgical Research 154: 38-44, 2009.

--Girardin CM, Deal C, Lemyre E, Lumbroso R, Beitel LK, **Trifiro MA**, Van Vliet G. Molecular studies of a patient with complete androgen insensitivity and a 47,XXY karyotype. J Pediatrics 155: 439-443, 2009.

--Anand SM, Gologan O, Rochon L, Tamilia M, How J, Hier MP, Black MJ, Richardson K, Hakami HA, Marzouki HZ, **Trifiro M**, Tabah R, Payne RJ. The role of sentinel lymph node biopsy in differentiated thyroid carcinoma. Arch Otolaryngol Head Neck Surg 135:1199-204, 2009.

--Gottlieb B, Beitel LK, Alvarado C, **Trifiro M**. Selection and mutation in the "new" genetics: An emerging hypothesis. Human Genetics 127: 491-501, 2010.

Richards, John Brent

--Mangino M, Richards JB, Soranzo N, Zhai G, Aviv A, Valdes AM, Samani NJ, Deloukas P, Spector TD. A genome-wide association study identifies a novel locus on chromosome 18q12.2 influencing white cell telomere length. J Med Gen, In Press Feb.6,

2009.

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--JB Richards, D Waterworth, S O'Rahilly, MF Hivert, RJF Loos, JRB Perry, T Tanaka, NJ Timpson, RK Semple, N Soranzo, K Song, N Rocha, E Grundberg, J Dupuis, JC Florez, C Langenberg, I Prokopenko, R Saxena, R Sladek, Y Aulchenko, D Evans, G Waeber, J Erdmann, M-S Burnett, N Sattar, J Devaney, C Willenborg, GIANT Consortium, A Hingorani, JCM Witteman, P Vollenweider, C Hengstenberg, L Ferrucci, D Melzer, K Stark, J Deanfield, J Winogradow, M Grassl, AS Hall, JM Egan, JR Thompson, SL Ricketts, IR König, W Reinhard, S Grundy, H-E Wichmann, P Barter, R Mahley, A Kesaniemi, DJ Rader, MP Reilly, SE Epstein, AFR Stewart, CM Van Duijn, H Schunkert, K Burling, P Deloukas, T Pastinen, NJ Samani, R McPherson, G Davey Smith, TM Frayling, NJ Wareham, JB Meigs, V Mooser,* TD Spector.* A genome-wide association study reveals variants in ARL that influence adiponectin levels. PLoS Genetics. 2009 Dec;5(12):e1000768. Epub.

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Oostra, HA Pols, G Sigurdsson, U Thorsteinsdottir, N Soranzo, FM Williams, Y Cupples, SH Ralston, G Thorleifsson, CM van Duijn DP Kiel, KS MD, AG Uitterlinden, JP Ioannidis, TD Spector, A Systematic Evaluation of 150 Candidate Genes for their Association with Osteoporosis and Osteoporotic Fracture in a Meta-Analysis of Genome-Wide Association Data. Annals of Internal Medicine. 2009 Oct 20;151(8):528-37.

--F Rivadeneira,* U Styrkársdóttir,* K Estrada,* B Halldórsson,* YH Hsu,* JB Richards,* MC Zillikens,* FK. Kavvoura, N Amin, YS Aulchenko, LA Cupples, P Deloukas, S Demissie, E Grundberg, A Hofman, A Kong, D Karasik, JB van Meurs, B Oostra, T Pastinen, HAP Pols, G Sigurdsson, N Soranzo, G Thorleifsson, U Thorsteinsdottir, FMK Williams, SG Wilson, Y Zhou, SH Ralston, CM van Duijn, T Spector, DP Kiel, K Stefansson, JPA Ioannidis, AG Uitterlinden, for the GEFOS Consortium. Twenty bone mineral density loci identified by large-scale meta-analysis of genome-wide association studies. Nature Genetics. 2009 Nov;41(11):1199-206. Epub 2009 Oct 4.

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Hakim, Elaine Dennison, Yongmei Liu, Chris Power, Helen E. Stevens, Laitinen Jaana, Ramachandran S. Vasan, Nicole Soranzo, Joerg Bojunga, Bruce M. Psaty, Mattias Lorentzon, Tatiana Foroud, Tamara B. Harris, Albert Hofman, JohnOlov Jansson, Jane A. Cauley, Andre G. Uitterlinden, Quince Gibson, Leena Palotie, David Karasik, David S. Siscovick, Michael J. Econs, Stephen B. Kritchevsky, Jose C. Florez,, John A. Todd*, Josee Dupuis*, Elina Hypponen*, Timothy D. Spector*. Common genetic determinants of vitamin D insufficiency: the SUNLIGHT consortium. The Lancet, epub June 10, 2010

Beitel, Lenore

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--Girardin CM, Deal C, Lemyre E, Lumbroso R, **Beitel LK**, Trifiro MA, Van Vliet G. Molecular studies of a patient with complete androgen insensitivity and a 47,XXY karyotype. J Pediatrics 155: 439-443, 2009.

--Gottlieb B, **Beitel LK**, Alvarado C, Trifiro M. Selection and mutation in the "new" genetics: An emerging hypothesis. Human Genetics 127: 491-501, 2010.

Abstracts

Richards, John Brent

--Richards JB, Kavvoura FK, Rivadeneira F, Styrkarsdottir U, Estrada K, Halldorsson BV, Hsu Y, Zillikens MC, Wilson SG, Mullin BH, Amin N, Aulchenko YS, Cupples LA, Deloukas P, Demissie S, Hofman A, Kong A, Karasik D, van Meurs JB, Oostra BA, Pols HAP, Sigurdsson G, Thorsteinsdottir U, Soranzo N, Williams FMK, Zhou Y, Ralston SH, Thorleifsson G, van Duijn CM, Kiel DP, Stefansson K, Uitterlinden AG, Ioannidis JPA, Spector TD for the Genetic Factors for Osteoporosis (GEFOS) Consortium. A systematic evaluation of 147 candidate genes for their association with osteoporosis and osteoporotic fracture in a Meta-Analysis of genome-wide association data. Podium presentation European calcified tissue society March 22, Barcelona, 2009.

--Richards JB, Hivert MF et al. Genome-wide association study reveals genetic variants in ARL15 associated with adiponectin levels and coronary heart disease. McGill University Endocrine Division Annual Retreat, Podium Presentation. May 14, 2009.

III OBJECTIVES AND PRIORITIES

The Division of Endocrinology continues to place a high priority on patient care and in doing so seeks new clinical recruits either as full-time or as part time members. Efforts are being made to

add another diabetic nurse to help with the ever-increasing referral of diabetic patients. Plans have been put forth to acquire new physical space that will help with delivering the excellent care that has been provided to-date with very limited space.

Other priorities include the expansion of both clinical research and basic research personnel that will start in the next few years. This will be a very arduous task given the many roadblocks at the university, government and hospital level; however the Division remains confident that when the right recruits come along, it will find the mechanisms to have them join its staff.

Respectfully submitted,

Marc Trifiro, MD
Chief, Division of Endocrinology